The Pending Claims

Claims 1-11 stand rejected. To these claims, applicant has added new claims 12-16 by way of the present Amendment.

The Office Action

Claims 1-10 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Claims 1 and 5-11 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Uematsu *et al.* (EP 0757106). Claims 2-4 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Uematsu *et al.* in view of Koller (USP 5,128,247) and/or Chomczynski (USP 5,945,515).

Discussion of the Claim Amendments

Claim 1 has been amended to add the phrase "thereby separating the nucleic acid from the test sample" as suggested by the Examiner. This claim amendment has support, *inter alia*, in the preamble of the amended claim. Claim 1 has also been amended to replace the second occurrence of the word "with" with the word --and--. This claim amendment is fully supported in the specification, for example, at page 2, lines 20-24.

Claim 9 has been amended to more clearly point out that the sources recited in the claim as originally filed are distinct from each other, e.g., from different types of viruses, bacteria, and/or cells. This claim amendment has support throughout the specification, including for example originally filed claim 9, Examples 5 and 6, and page 2, lines 27-28.

Claim 10 has been amended solely to better comport gramatically with amended claim 9.

Claim 11 has been amended so that it now recites that nucleic acids form nucleic acid/metal oxide complexes when the metal oxide particles are contacted with nucleic acids. This claim amendment is supported throughout the specification, e.g., in originally filed claim 1.

New claim 12 is directed to the method of claim 8 wherein the step of amplifying the nucleic acid is performed without removing the elution buffer. This claim has support in the specification, e.g., at page 3, lines 21-25.

New claims 13 and 14 are directed to particular embodiments of the present invention wherein the pH of the elution buffer is of between 6 and 10, or 7 and 9, respectively. Support for these claim amendments can be found in the specification, e.g., at page 7, lines 1-2.

New claims 15 and 16 are directed to particular embodiments of the present invention wherein the elution buffer comprises between 10 mM and 300 mM phosphate, or 10 mM and 100 mM phosphate, respectively. Support for these claim amendments can be found in the specification, e.g., at page 6, lines 25-29.

Discussion of the Indefiniteness Rejection

The Office Action alleges that claims 1-10, as originally filed, were impermissibly indefinite because the body of claim 1 did not terminate with a positive process step which clearly related back to the preamble. The Examiner suggested curing this alleged deficiency by amending claim 1 to include the phrase "thereby separating the nucleic acid from a test sample." Applicant has adopted the Examiner's suggestion, which appears to obviate the instant rejection.

The Office Action also alleges that claims 1-10, as originally filed, were impermissibly indefinite because claim 1 recited contacting the test sample "with a metal oxide support material with a binding buffer." Claim 1 as now pending does not contain this typographical error and tracks the language of page 2, lines 20-24. Accordingly, applicant submits that claims 1-10, as pending, are definite.

The Office Action also alleges that claims 9 and 10, as originally filed, were impermissibly indefinite because the claims allegedly did not make clear from what the sources were distinct. Claims 9 and 10 as pending are not susceptible to this alleged source of indefiniteness, because they do not recite the phrase "distinct sources."

Applicant, therefore, requests withdrawal of the indefiniteness rejection.

Discussion of the Anticipation Rejection

Claims 1 and 5-11 stand rejected as allegedly being anticipated by Uematsu *et al*. Applicant respectfully traverses the anticipation rejection.

Claim 1, recites that the test sample is contacted "with a metal oxide support material and a binding buffer *to form nucleic acid/metal oxide support material complexes*." That is, the present invention as defined by claim 1 requires the nucleic acid *in a test sample* to complex with a metal oxide.

In contrast, Uematsu *et al*. discloses the use of magnetic-responsive particles that are coated with a substance, and it is the coating that bonds with nucleic acids. Uematsu *et al*. does

not disclose a method of separating nucleic acid from a test sample that comprises the formation of a metal oxide/nucleic acid complex.

Specifically, Uematsu *et al.* discloses multiple categories of magnetic responsive particles. First, Uematsu *et al.* discloses the use of magnetic-responsive particles that contain a metal oxide (i.e., iron oxide) "core covered with a polymeric silane layer" (page 2, lines 8-10). Uematsu *et al.* also discloses a metal oxide core covered with "a biocompatible molecule (for example, a nucleic acid)" (page 2, lines 19-20), and a metal oxide core covered with nitrocellulose (page 2, lines 21-26). In another alternative, Uematsu *et al.* discloses the use of a poly-cationic substrate covering a solid support (page 2, lines 28-29). In a final alternative, Uematsu *et al.* discloses a particle comprising three layers; the first layer is an inner core of a polymer such as polystyrene, which is covered by a medial layer comprising a mixture of a polymer and a metal oxide, which in turn is covered by a layer of covalently bound probe used to bind to nucleic acids (page 2, lines 38-52). Moreover, the focus of the Uematsu *et al.* reference appears to be silica-covered magnetic particles (page 3, lines 26-30, especially in view of page 2, lines 8-10). In each of these cases, the metal oxide, which permits separation of the particle from a sample by use of a magnetic field, is covered with a substance that binds with nucleic acid in a sample or source. In no case does Uematsu *et al.* disclose that it is the metal oxide that complexes with nucleic acid. Accordingly, Uematsu *et al.* fails to teach or reasonably suggest the subject matter of claim 1.

Pending claims 2-10 and 12-16 depend directly or indirectly from claim 1. Therefore, the subject matter defined by claims 2-10 and 12-16, by definition, is encompassed within the subject matter of claim 1. Since Uematsu *et al.* fails to teach or reasonably suggest the subject matter of claim 1, Uematsu *et al.* also fails to teach or disclose the subject matter of pending claims 2-10 and 12-16.

Claim 11, as pending, recites that the metal oxide particles are capable of reversibly forming metal oxide/nucleic acid complexes when contacted with nucleic acid in a test sample. As discussed above with respect to claim 1, Uematsu *et al.* does not disclose a metal oxide particle capable of forming a metal oxide/nucleic acid complex. Accordingly, Uematsu *et al.* does not teach or reasonably suggest the subject matter of claim 11.

Discussion of the Obviousness Rejection

A. Uematsu et al. in view of Koller

The Office Action alleges that the disclosure Uematsu *et al.* taken in view of Koller demonstrates that the subject matter of claim 2 would have been obvious to the ordinarily skilled artisan at the time of applicant's invention. Applicant respectfully traverses the rejection.

The Uematsu *et al.* reference, which is discussed above, does not support the obviousness rejection at least for essentially the same reasons that Uematsu *et al.* does not support the anticipation rejection.

The Office Action cited Koller merely to allege that the use of chaotropic compounds and reducing agents in nucleic acid releasing buffers and nucleic acid binding buffers are known in the prior art.

Claim 2 depends from claim 1, which requires the formation of nucleic acid/metal oxide support material complexes. However, as discussed above with respect to the anticipation rejection, Uematsu *et al.* fails to teach or reasonably suggest a method of separating nucleic acid from a test sample comprising the formation of a nucleic acid/metal oxide complex. Nothing in Koller cures this failure of Uematsu *et al.* to teach or reasonably suggest the present invention. In this regard, Koller is silent with respect to the use of particles to separate nucleic acids from test samples and instead suggests the use of precipitation (column 7, line 12, to column 8, line 27). Therefore, applicant respectfully requests the withdrawal of the obviousness rejection predicated on the combination of Uematsu *et al.* and Koller.

B. Uematsu et al. in view of Chomczynski

The Office Action alleges that the disclosure Uematsu *et al.* taken in view of Chomczynski demonstrates that the subject matter of claims 2-4 would have been obvious to the ordinarily skilled artisan at the time of applicant's invention. Applicant respectfully traverses the rejection.

Uematsu *et al.* is discussed above.

Chomczynski, like Uematsu *et al.*, does not disclose a method of separating nucleic acid from a test sample that comprises the formation of nucleic acid/metal oxide complexes. In this regard, Chomczynski suggests the use of (selective) precipitation to isolate and separate nucleic acids from a sample (paragraph bridging columns 4 and 5), rather than the use of nucleic

acid/metal oxide complex formation and subsequent elution. Accordingly, applicant respectfully requests the withdrawal of the obviousness rejection of claims 2-4 predicated on the combination of Uematsu *et al.* and Chomczynski.

Additionally, and with respect to claim 3, the Office Action alleges that Chomczynski discloses a binding buffer with low concentrations of alcohol that would be expected to have a flashpoint of greater than 130° F. Applicant has examined Chomczynski, but has been unable to identify any explicit teaching or reasonable suggestion that any buffer disclosed therein has a flashpoint of greater than 130° F. Accordingly, even if there is reason to maintain the obviousness rejection of claims 2 and 4, the obviousness rejection of claim 3 should be withdrawn.

Conclusion

The Examiner is requested to pass the present application to allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the present application, the Examiner is invited to call applicant's undersigned representative.

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Respectfully submitted,
G. Gundling

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